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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/005,710	11/08/2001	Aristo Vojdani	IMSC12.004A	7714

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EXAMINER
NGUYEN, BAO THUY L

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/27/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/005,710	VOJDANI, ARISTO	
	Examiner	Art Unit	
	Bao-Thuy L. Nguyen	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *11/15/04 & 12/23/04*
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 April 2005 has been entered.

2. Claim 2 has been canceled. Claims 1 and 3-6 are pending.

3. All rejections not reiterated herein below are withdrawn in view of the amendments to the claims.

Election/Restrictions

4. Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, the species of myosin, heat shock protein-60, β-2-glycoprotein-1, platelet glycoprotein, and C1q immune complexes are withdrawn as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

5. Claims 1, 3-6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 contains limitations that were non-elected.

Claim Rejections - 35 USC § 103

6. Claims 1 and 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kovanen et al (*Archives of Internal Medicine*. July 13, 1998. Vol. 158, No. 13, pages 1434-1439, IDS) in view of Stone et al., (*Journal of Human Stress*. 1987. Vol. 13, pages 136-140).

Kovanen discloses elevated levels of IgA, IgE and IgG in patients with established arteriosclerosis and myocardial infarction or cardiac death. See page 1435. Kovanen discloses autoantigens and several exogenous antigens as having been implicated in the pathogenesis of myocardial infarction including oxidized LDL and cardiolipin. See page 1437.

Kovanen differs from the instant invention in failing to teach the detection of IgA in saliva.

Stone, however, teaches the measurement of IgA antibody response to a particular antigen in saliva using ELISA. Stone teaches that although IgA is also present in serum, secretory IgA (sIgA) is more advantageous in that it is much larger

and binds invading organisms more effectively than serum IgA. Stone also teaches that sIgA can be collected rather simply and inexpensively in saliva and quantitated with a readily available assay. See page 138.

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to use the method of Kovanen to measure sIgA and relating the measured level with diseases such as cardiovascular disease because Stone teaches that sIgA can be measured with ease and the level of sIgA can be directly correlated with immunocompetence. The collection of samples such as saliva is simple and painless and the measurement of sIgA against a specific antigen provides the advantage of a method that has few problems and provides a more meaningful assessment of the sIgA system.

Response to Arguments

7. Applicant's arguments filed 20 April 2005 have been fully considered but they are not persuasive.

Applicant argues that there is no motivation to combine the teachings of Kovanen with Stone because Kovanen fails to recognize the importance of saliva as a source of IgA antibodies against autoantigens and Stone does not teach that there is a proportional relationship between serum and saliva IgA antibodies. Applicant also argues that Stone does not teach that sIgA is related to the presence or possibility of cardiovascular disease.

These arguments have been fully considered but are not deemed to be persuasive. Kovanen specifically teaches that IgA against oxidized LDL (oLDL) and cardiolipin can be detected, and related to the pathogenesis of MI. Kovanen discloses that total levels of antibodies have been determined in patients with atherothrombotic disease and patients with established atherosclerosis have significantly elevated levels of IgA, IgE, IgG and IgM. Clearly, Kovanen recognizes the importance of the presence of IgA against oLDL in body fluids and its relationship to cardiovascular diseases.

Stone, on the other hand, discloses that the immunocompetence of an individual can be assessed using the secretory components such as IgA. Stone teaches that sIGA can be collected simply and inexpensively in saliva and quantitated with a readily available assay. Although, it is true that Stone discloses that serum IgA and sIgA are different from each other, specifically sIgA is much larger than serum IgA, this difference is not seen to be an inhibiting factor in detecting sIgA against autoantigens. In fact, one of ordinary skill in the art would have been motivated to use saliva as a sample not only because of the ease with which it can be collected, but also because the larger sIgA would have been more easily detected.

Applicant asserts that there is conflicting reports about the usefulness of detecting antibody immune status using samples such as saliva and feces and asserts that Externest et al proves this point. Applicant argues that Externest concludes that any relationship between serum, saliva or urine IgA level as a predictor of other sIgA release is dependence on antigen type and dosage. Thus, the uncertainty of the

relationship between secretory and serum IgA would not suggest to one of ordinary skill in the art that it would be advisable to combine the teaching of Kovanen and Stone.

This argument is not persuasive. Kovanen clearly teaches that elevated levels of IgA, IgE or IgG to oxidized LDL are associated with myocardial infarction and cardiac death. Externest, on the other hand, teaches that sIgA is a powerful means to protect against enteric pathogens and that this is well recognized in the art. Specifically, Externest teaches that specific antibody responses against different antigens were detected in humoral, secretions, and excretions samples. See page 3830, second column first full paragraph. Contrary to the assertion that Externest teaches that there is confusion about the usefulness of easy to sample specimens such as saliva and feces in assay to detect antibody immune status, Externest teaches that anti-Ct serum IgG, and IgA as well as fecal IgA were readily detectable and that the general shape of the immune response curves was identical for all of these groups. See page 3832, second column, first full paragraph. Externest also teaches that when comparison is made between these groups, an almost linear relation between antigen dosage (i.e. the immunized dose) and the resulting group mean IgA responses were observed for all sites. See page 3833, first column, second full paragraph. It is true that Externest teaches that there is a strong correlations between specific antibody responses at different effector sites and the type and dose of antigen used when immunizing the animal; however, this does not teach away from using saliva IgA as an indicator, it just mean that one must take into consideration the type of antigen to which the IgA is

directed. As a matter of fact, Externest provides the motivation for one to use sIgA because the response of mucosal vaccines, for example, would be a rapid and cheap method for mass screening. Externest teaches that the high relative amount of specific IgA in urine is not different from that in serum, intestinal secretions, or feces substantiates the concept of using sIgA to detect immune status. See page 3835, second column, first full paragraph.

Given these teaching, it is maintained that a skilled artisan would have had a reasonable expectation of success in combining the teachings of Kovanen and Stone.

Conclusion

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bao-Thuy L. Nguyen whose telephone number is (571) 272-0824. The examiner can normally be reached on Tuesday and Thursday from 8:00 a.m. -3:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Bao-Thuy L. Nguyen
Primary Examiner
Art Unit 1641
6/23/05